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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	20

DATE MAILED: 08/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/668,788	WOLTER ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,6,18-20 and 22-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,6,18-20,22-38 and 40-44* is/are rejected.

7)☒ Claim(s) *39* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *00857* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *17* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-3, 5-6, 18-20, 22-44 are still at issue and are present for examination.

Applicants' amendments and arguments filed on 5-28-03, paper No.19, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 19 recites a limitation, i.e., "processive lipid glycosyl transferase" which is much broader than the limitation "processive diacylglycerol glycosyltransferase" of claim 1 from which claim 9 depends from, rendering it indefinite.

Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 32 recites a limitation, i.e., " bacterial processive lipid glycosyl transferase" which is much broader than the limitation "bacterial processive diacylglycerol glycosyl-transferase" of claim 27 from which claim 32 depends from, rendering it indefinite.

Claims 40-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 40 is directed to a method of production of glycolipids using a processive lipid glycosyl transferase that successively transfers a hexose residue to a lipid acceptor comprising the steps of obtaining a polynucleotide that encodes said activity followed by expressing said protein to produce said glycolipids. The metes and bounds of the phrase "expressing the protein" is highly unclear to the Examiner. It is not clear to the Examiner whether expressing the protein involves only transforming a cell that can express said protein with the polynucleotide that encodes said polypeptide and activity or does the scope of the claim involve anything other than that, rendering the claim indefinite.

Claims 26 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 26 and 43 are drawn to a process of glycosyl compounds using PDGs comprising an amino acid sequence selected from a group of peptides. The claim also recites phrases such as "more than 5 amino acids from within the sequence..." and more than 6 amino acids with in the sequence..". The above phrases render the claims indefinite because it is not clear to the Examiner whether these 5 and 6 amino acids from within the sequences mentioned need to be consecutive or simply comprise any 5 or any 6 amino acids from within the sequence in random order. Without such information, the claim is rendered indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-6, 18-20, 22-38, 40-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process of making specific glycolipids using processive diacylglycerol glycosyltransferase (PDG) enzymes with amino acid sequence SEQ ID NO:2 or 4, does not reasonably provide enablement for such a process using any PDG from any or all sources or using any PDG enzyme isolated from any strain of *B.subtilis* or *S.aureus* or any PDG enzyme having an amino acid sequence that is either 70%, 80%, 90%, 95% identical to SEQ ID NO:2 or 4 including fragments of such enzyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-3, 5-6, 18-20, 22-38, 40-44 are so broad as to encompass a process which uses any PDG or any lipid glycosyltransferase from any strain of *B.subtilis* or *S.aureus* or any PDG from any source including recombinants, variants and mutants. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large

number of lipid glycosyltransferases and PDGs broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence to obtain the desired activity, requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim. The disclosure is limited to a process in which the amino acid sequences of only two PDGs are used.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen multiple sources or to screen for multiple substitutions or multiple modifications, or as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any lipid glycosyltransferases or PDGs from any or all sources or any PDGs of any strain of *B.subtilis* or *S.aureus* because the specification does not establish: (A) a rational and predictable scheme for isolating and using any lipid glycosyltransferase/PDG from any source; (B) regions of any or all lipid glycosyltransferase/PDG protein structure which may be modified without effecting its activity; (C) the general tolerance of lipid glycosyltransferases/PDGs to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any amino acid residue in any lipid glycosyltransferase/PDG with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including all or any PDG from any and all sources. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of lipid glycosyltransferases/PDGs having the desired enzymatic characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re* Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants have traversed the above rejection. Applicants assert that claims are enabled because the skilled artisan can easily make and the use the PDG enzyme without undue experimentation. Quoting from *Wands*, applicants conclude that

experimentation necessary is merely routine and their specification provides ample guidance on the experimentation. Applicants argue that procedures for isolating, cloning characterizing and using nucleic acids encoding a PDG are all provided in the specification. Applicants argue that source organisms have also been provided in the specification along with PCR primers and two working examples which illustrate cloning and expression of PDG from bacteria. While it is agreed that specification provides all the above information, claims are drawn to methods in which lipid glycosyltransferases isolated from any source and enzymes that are anywhere from 70% to 95% identical SEQ ID NO:2 or 4 and enzymes comprising fragments of specific amino acids are to be used and applicants are silent on the aspects of how one skilled in the art can arrive at all these sequences including variant sequences without any guidance for making the amino acid changes. While claims are directed to the methods in which any lipid glycosyltransferase or PDGs can be used, claims are also directed to methods wherein variants or mutants that differ in amino acid sequences from SEQ ID NO:2 or 4 are to be used. Nowhere in the specification, does applicant provide guidance as to how one skilled in the art can go around to make changes in the amino acid sequences and arrive at enzymes that have 70% to 95% sequence identity with SEQ ID NO:2 or 4 and use such enzymes in the above process.

Applicants also argue that they were the first to recognize the processive property of the above enzymes whose amino acid sequences were already well known in the art and whose activity was known to be just glycosyltransferase activity (non-processive). However, applicants have not demonstrated this property from enzymes isolated from at least a representative number of sources from among the extremely large number of biological sources. To their credit they have provided only two examples. Contrary to their conclusion, information from

just two examples cannot be taken as representative information of such an enzyme from all other varied sources.

Applicants also dispute the reference of Saxena et al. alleging that nowhere does Saxena et al. describe glycosyl transferases that transfer to lipid acceptors. Examiner respectfully disagrees with such mischaracterization of the reference and urges applicants to peruse the reference again specifically at lines 5-6 in column 1, page 1419 wherein it clearly states that acceptors of the hexose sugars can also be lipid carriers. It is not clear to the Examiner as to how the reference of Koyama et al. is persuasive to overcome the above rejection.

Therefore contrary to applicants argument that the specification is enabled for the above claims, the specification totally lacks guidance as to how one of skilled in the art can isolate and characterize the enzyme from any or all sources, make changes to the amino acid sequences of SEQ ID NO:2 or 4 and use such modified amino acid sequences in the method that is claimed. Amended claims continue to be directed to any and all lipid glycosyltransferases isolated from any or all sources and applicants have not provided guidance to isolate and characterize such an enzyme from any or all sources which includes all microorganisms, plants, animals and viruses. Applicants' arguments are also not persuasive to overcome the above rejection because while methods to produce variants of a known amino acid sequence, such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan, producing variants as claimed by applicants requires that one of ordinary skill in the art know or be provided with guidance with reference to specific amino acid positions whose alteration does not alter the property of the enzyme and also which specific variant among the extremely large number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity

of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting PDG transferase activity; (B) the general tolerance of PDG transferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue in the amino acid sequence of the above enzyme with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Therefore the above rejection is maintained.

Claims 22-26, 36-38, 40-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process of making specific glycolipids using processive diacylglycerol glycosyltransferase (PDG) enzymes with amino acid sequence SEQ ID NO:2 or 4, does not reasonably provide enablement for such a process using any processive lipid glycosyltransferase (PLG) from any or all sources or any PLG enzyme having an amino acid sequence that is either 70%, 80%, 90%, 95% identical to SEQ ID NO:2 or 4 including fragments of such enzyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 22-26, 36-38, 40-42 are so broad as to encompass any PLG from any source or having an amino acid sequence that is either 70%, 80%, 90%, 95% identical to SEQ ID NO:2 or 4 including fragments of such enzyme. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of PLGs broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only two PDGs but not to any PLG. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching the use of SEQ ID NO: 2 and 4 as a processive diacylglycerol glycosyltransferase but provides no guidance with regard to the making of variants and mutants or with regard to the use of any PLG as a PDG. In view of the great breadth of the claim, amount of experimentation required to make the claimed

polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any PLG with 70%, 80%, 90% or 95% identity to the enzymes of SEQ ID NOS:2 and 4 because the specification does not establish: (A) that all or any PLG will also have the property of a PDG; (B)regions of any PLG protein structure which may be modified such that it would have PDG activity; (B) the general tolerance of any or all PLGs to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue on any PLG with an expectation of obtaining the desired PDG function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including all or any PLGs to have the property of PDG with an enormous number of amino acid modifications in SEQ ID NOS: 2 and 4. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of PLGs having the desired biological characteristics as PDGs is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1-3, 5-6, 18-20, 26-35, 43-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3, 5-6, 18-20, 26-35, 43-44 are directed to a process of producing glycolipids using any processive PLG/PDG or using any bacterial PLG/PDG or fragments of PLGs. Claims are rejected under this section of 35 USC 112 because the claims are directed to a process of producing any glycolipid using a genus of polypeptides that have not been disclosed in the specification. No description has been provided of the polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:2 or 4 for the above purpose has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of

the structure of all the polypeptide sequences encompassed by the claims, including fragments and variants within the scope of the claimed genus. The genus of polypeptides used in the claims is a large variable genus including peptides and polypeptides which can have a wide variety of structure. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses a method of making glycolipids using only two species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office action applicants have traversed the above rejection arguing and asserting that specification provides ample teaching to describe the full scope of the claims. Applicants recite a number of court cases and court decisions. However, it is beyond the scope of this Office action to respond to each of those court cases without the knowledge of the claims involved and the prosecution history of those applications. In summary, and according to applicants own conclusion "functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics" is sufficient to satisfy the requirements of 35 U.S.C. 112, first paragraph" (see page 20 end of first para of response).

Applicants vehemently argue that specification sufficiently describes identifying characteristics to distinguish the claimed invention and to show possession at the time of filing. Examiner respectfully disagrees with such a conclusion. Applicants argue that specification describes "several working examples of nucleic acids" (page 20, line 10, of response) and provide only two examples, SEQ ID NO:1 and 3. Applicants also argue that specification provides several partial sequences referring to the 8-12 amino acid fragment sequences of a protein that is at least 382 amino acids in length which is to be construed as structural characteristic of the entire protein. Examiner respectfully disagrees with such an argument as being persuasive of overcoming the above rejection. In that regard applicants attention is drawn to the rejection of claims 26 and 43 below. Applicants also argue that specification provides working examples and partial sequences along with assays and techniques for analyzing and characterizing the activity and that these routine assays permit the skilled artisan to distinguish members of the claimed genus. Applicants also argue that the scope of the claims have been amended to limit to a process for production of specific glycolipids and the combination of these teachings will demonstrate to the skilled artisan that applicants possessed the full genus of the PDGs at the time of filing of the instant application. Examiner respectfully disagrees with such an argument to be persuasive to overcome the above rejection. This is because, while the specification teaches assay techniques etc. it teaches only two species of the entire genus of polypeptides claimed. Furthermore, the structural feature provided by means of very short fragments of amino acid sequences cannot be considered as representative of the entire genus (see below). As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a

representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only two species within the genus or just very short fragments of an amino acid sequence of significant length . In the instant case the claimed genera of claims 1-3, 5-6, 18-20, 26-35, 43-44 includes species which are widely variant in structure. The genus of claims 1-3, 5-6, 18-20, 26-35, 43-44 is structurally diverse as it encompasses polypeptides with PDG activity from any or all sources including mutants, variants recombinants. As such, neither the description of the structure of SEQ ID NOS:2 and 4 or 5-10 nor the disclosure of solely functional features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus. Therefore the above rejection is maintained.

Claims 26 and 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of PLGs/PDGs with specific 8 or 12 amino acid long peptide sequences (SEQ ID NO:5-10), and 5-6 amino acid sub-fragments of the same. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification teaches the isolation and characterization of only two species PDGs, i.e., SEQ ID NO:2 or 4. Moreover, the specification fails to describe any other representative species by sufficient identifying characteristics or properties to show that applicant was in possession of the claimed genus. The identifying characteristics recited in Claim 26 or 43, i.e., just the enzymatic activity, processive lipid glycosyltransferase or processive diacylglycerols glycosyltransferase (but with no other characteristics such as a molecular weight or optimum pH or temperature, specific inhibitors or enhancers, metal ions

requirements etc.), does not include sufficient characteristics to limit the claimed genus to proteins which are not highly variable in both structure and function. The claims include species in which 97% of the amino acid sequence of the disclosed species has been substituted as well as allowing alterations in functional characteristics such as substrate specificity, temperature optima, pH optima, and inhibitor/activator profiles. Therefore, the species within the genus are highly variable in both structure and function. Just the characteristics of the function of the enzyme combined with the amino acid sequence of very short fragments of 8 or 12 amino acids, by itself is not sufficient to change the fact that the claims include proteins which are highly variable in both structure and function. Thus for all the reasons discussed, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Conclusion

None of the claims except for claim 39, are allowable.

Claim 39 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Examiner has withdrawn the objection to the specification for introduction of new matter as applicants have demonstrated that said matter was not new but part of the specification as originally filed. Examiner has withdrawn the rejection of claims 1-3, 22-23 under 35 U.S.C. 112, Ist paragraph as applicants have limited the claims to method of making specific glycolipids.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 7:30 a.m. to 4:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Manjunath N. Rao, Ph.D.
8/2/03

MANJUNATH RAO
PATENT EXAMINER